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10/018,834	12/19/2001	Eric Edward Worrall	STHP002	4441

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/018,834

Applicant(s)

WORRALL, ERIC EDWARD

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 12-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## DETAILED ACTION

### *Status of the Claims*

1. In the prior action (mailed March 25, 2003), claims 1-6, 20, and 22 were rejected, and claims 7-19, 21, and 23-26 were objected to. In the Response filed on September 11m 2003, the Applicant amended claims 1, 4, 7, 8, 12-14, 26-28, and 21-28, cancelled claim 11, and added new claims 27-49. Claims 1-10, and 12-49 are currently pending and under consideration.
2. Because this action raises new rejection not necessitated by amendment, it is being made Non-Final.

### *Claim Objections*

3. Claims 7-19, 21, and 23-26 were objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependant claim. See MPEP § 608.01(n). In view of the amendment to the claims, the objection is withdrawn.

### *Claim Rejections - 35 USC § 112*

4. **(Prior Rejection- Withdrawn)** Claims 1-6 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendment of the claim, the rejection is withdrawn.
5. **(Prior Rejection- Withdrawn)** Claim 4 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

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distinctly claim the subject matter which applicant regards as the invention. In view of the amendment of the claim, the rejection is withdrawn.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. **(New Rejection-Necessitated by Amendment)** Claims 13-26, and 37-49 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In describing the second drying procedure of the preservation method, these claims describe the step as occurring "at a temperature which finally is in the range of from 40-45° C. It is unclear what is meant by the inclusion of the term "finally" in the phrase. For example, does the inclusion of this term allow for random temperature fluctuation until the end of the drying phase, or is there a steady increase or decrease in temperature from an undisclosed initial temperature. Clarification is required.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. **(Prior Rejection- Maintained in part)** Claims 1-3, 5, 6, 20, and 22 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653

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(Roser I), in view of Illum et al. (U.S. Patent 6,391,318) and Chatfield (U.S. Patent 6,136,606), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II). The Applicant traversed this rejection on the grounds that the identified combination of references does not teach the claimed invention in that the references do not teach a step of forming a coacervate of chitosan and the bioactive material prior to addition or trehalose. The traversal is persuasive as to the method claims, claims 1-3, 5, and 6, the rejection is therefore withdrawn as to these claims.

However, because the composition claims, claims 20 and 22, and amended claims 21, 23, 24, 25, and 26, do not anywhere limit the composition to the inclusion of a coacervate, or describe any particular relationship between the chitosan and the bioactive material. Thus, the identified composition claims do not include structural features that distinguish from the composition that would result from the identified combination of references. Because the Rosen reference teaches the use of the disclosed method for any vaccine, and because the references indicate that chitosan is an effective vaccine adjuvant, it would have been obvious to those in the art to make the claimed compositions.

10. **(New Rejection)** Claims 1-3, 5-10, 12-14, 16-25, 27-29, 31, 33-39, 41-43, 45-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653 (Roser I), in view of Illum et al. (U.S. Patent 6,391,318) and Chatfield (U.S. Patent 6,136,606), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II), and further in light of the teachings of Herbert et al (U.S. Patent 5,654,008) and Orly et al. (US Patent 5,672,301). As indicated above, claims 1-3, 5, 6, 20, and 22 were rejected in the prior

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action under 35 U.S.C. 103(a) as being unpatentable over Roser I, in view of Illum and Chatfield, and in view of Roser PCT and Roser II. Thus, the claims and the references, other than Herbert and Gander, have been described in the prior action. It is noted that, at least with respect to certain types of biological materials, Roser I teaches preferred trehalose w/v measurements that are overlapping with, and render obvious the claimed ranges (as optimization of the described methods). See, column 2, lines 14-20. In the Response, the Applicant appears to have made two arguments in traversal of the rejection.

The Applicant's first argument in traversal is that there is no suggestion or teaching in the references to make a coacervate of the chitosan and the bioactive material prior to adding the trehalose to the composition for preservation. In view of this argument, the prior rejection was withdrawn and is restated as indicated above. As indicated in the prior action, each of Illum and Chatfield teach the use of chitosan as a vaccine adjuvant. Further. As indicated in claim 17 of Illum, it would have been obvious to those in the art to make chitosan/antigen compositions in the form of microparticles. Each of Chatfield and Illum additionally teach the combination of a 1:1 mixture of the chitosan and bioactive agent, however, they teach preferred ph of between 5 and 6.5, and not 7.4. The teachings of each of Herbert and Gander indicate that one method for making such microparticles comprising a bioactive agent is through making a coacervation of the agent and the polymer used to form the particle. See, Herbert, col 3, lines 27-31; and Orly, col. 1, lines 24-28, and claim 8. Thus, it would have been obvious to those in the art attempting to preserve a vaccine through freeze-drying to add trehalose to a microparticle coacervate of the antigen and chitosan to perform the drying described by the Roser references. The rejection is

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therefore maintained for reasons indicated in the prior action, in combination with the reasons above with reference to the newly added references.

The second argument is that the Roser I reference does not teach certain limitations of the claimed methods. In particular, the Applicant argues that this reference does not teach carrying out the drying procedure at a temperature at or below 37° C, and which may thereafter fall provided it does not fall to or below 0° C. However, as indicated in the prior action, the Examiner agrees that Roser does not provide such teachings, but believes that the Roser II and Roser PCT articles make up for these deficiencies. In particular, the temperature and pressure ranges indicated in the claims are rendered obvious by the teachings of Roser II as indicated in the prior action. See, Roser II, column 6, lines 15-25. While it is noted that Roser II relates to the preservation of platelets, the reference teaches that the method is useful for the preservation of these bioactive agents because it preserves functionality, and improves the stability, of the stored platelets. It would therefore have been obvious to those in the art to use the methods of preservation disclosed in this reference for the preservation of other compositions. For example, the more general methods of Roser PCT indicate that similarly low pressures and with a temperature of 40° C may be used to dry biological methods in general. Upon noting that this, and the fact that Roser II teaches the claimed ranges as improving the storability of a product with a limited storage capacity, those in the art would have had a reasonable expectation of success in the application of these pressure and temperatures to other bioactive materials as well.

Thus, this second argument in traversal is an argument based on a deficiency in one of the identified references in a rejection based on a plurality of references. Such an argument is not sufficient to overcome the rejection. See e.g., In re Keller, 208 USPQ 871 (CCPA 1981); and In

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re Merck & Co., 231 USPQ 375 (Fed. Cir. 1986) (each decision indicating that applicant cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references). For this reason, the reasons above, and for the reasons of record, claims 1-3, 5-10, 12, 20-26, 27, 28, 31, 33, and 36 are found obvious over the identified references.

Additionally, Roser PCT also teaches a secondary drying step that may be used in conjunction with the primary drying step. As described by the claims, this drying step may be conducted at pressures of about .05 Torr (less than .1 mbar) and at temperatures in the range of 15-45° C. Claims 29 and 33. Further, the reference teaches that it is preferable to conduct this secondary step at lower pressures so that lower temperatures (which protect the integrity of the biological material) may be used. Pages 16-17. Also, each of Roser I and II teach that the preferred trehalose w/v concentrations are about 1-20%, or 5-10%, ranges that overlap and render obvious the ranges in (e.g.) claims 8-10.

11. **(Prior Rejection-Restated)** Claim 4 was rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Roser I, in view of Illum, Chatfield, Roser PCT, and Roser II as applied to claims 1-3, 5, 6, 20, and 22 above, and further in view of Rweyemamu et al., *Revue Scientifique et technologique* 14(3), 593-601 (Medline abstract cited and provided) and Gombotz et al., U.S. Patent 5,900,238. For the reasons indicated above with respect to claims 1-3, 5-10, 12, 20-26, 27, 28, 31, 33, and 36, the rejection of claim 4 is restated as follows: claims 4, 26, 30, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser I, in view of Illum, Chatfield, Roser PCT, and Roser II, further in view of Rweyemamu and



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Gombotz, and in light of Herbert and Orly. The rejection is restated and maintained for the reasons indicated above, and for the reasons of record.

12. **(New Rejection)** Claims 1, 2, 5, 7-10, 2-14, 16-24, 27, 28, 31, 33-38, 41-43, and 45-48, are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653 (Roser I), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II), and further in view of the teachings of Roy et al., U.S. Patent 5,972,707. The claims and the teachings of the Roser references were described in the prior action. For the purposes of this rejection, it is assumed that the term vaccine includes DNA vaccines. In the presently rejected embodiment, the biological material is a nucleic acid. Roy teaches a composition for the delivery of a gene to a body comprising a coacervation of the nucleic acid with a polymeric cation, a preferred example of which is chitosan. Abstract, col. 4, lines 62-65, and cols. 9-10. Once the coacervate had been made, it would have been obvious to those in the art to use the methods disclosed by the Roser references to preserve the material until ready for use. See, e.g., Roser PCT, pages 11 and 12 (teaching that nucleic acids, among other materials, may be preserved using the disclosed methods). The references therefore render obvious the identified claims.

### ***Conclusion***

13. No claims are allowed.

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14. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.


Fernandez-Urrusuno teaches the use of chitosan microparticles for the delivery of proteins through the mucous membranes, and the freeze-drying of such particles. Abstract. The reference is considered redundant, in part, to the combined teachings of Illum and the Roser references.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Z. Lucas  
Patent Examiner

  
JAMES HOUSEL 12/1/03  
SUPERVISORY PATENT EXAMINER  
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